as a control for correlation of virus titers.

[38 FR 32068, Nov. 20, 1973, as amended at 49 FR 23834, June 8, 1984; 55 FR 11013, Mar. 26, 1990]

§ 630.54 Potency test.

The concentration of live mumps virus shall constitute the measure of potency. The titration shall be performed in a suitable cell culture system, free of wild viruses, using either the Reference Mumps Virus, Live, or a calibrated equivalent strain as a titration control. The concentration of live mumps virus contained in the vaccine of each lot under test shall be no less than the equivalent of 5,000 $TCID_{50}$ of the reference virus per human dose.

§ 630.55 Test for safety.

(a) *Tests prior to clarification.* Prior to clarification, the following tests shall be performed on each mumps virus pool prepared in chick embryo cell culture:

(1) *Inoculation of adult mice.* The test shall be performed in the volume and following the procedures prescribed in § 630.35(a)(1), and the virus pool is satisfactory only if equivalent test results are obtained.

(2) *Inoculation of suckling mice.* The test shall be performed in the volume and following the procedures prescribed in § 630.35(a)(2), and the virus pool is satisfactory only if equivalent test results are obtained.

(3) *Inoculation of monkey cell cultures.* A mumps virus pool shall be tested for adventitious agents in the volume and following the procedures prescribed in § 630.35(a)(3), and the virus pool is satisfactory only if equivalent test results are obtained.

(4) *Inoculation of other cell cultures.* The mumps virus pool shall be tested for adventitious agents in the volume and following the procedures prescribed in § 630.35(a)(3), in rhesus or cynomolgus monkey kidney, in whole chick embryo, and in human cell cultures. In addition, each virus pool shall be tested in chick embryo kidney in the same manner except that the volume tested in each cell culture shall be equivalent to 250 human doses or 25 milliliters, whichever represents a greater volume. The mumps virus pool is satisfactory only if results equivalent to those in § 630.35(a)(3) are obtained.

(5) *Inoculation of embryonated chicken eggs.* A neutralized suspension of each undiluted mumps virus pool shall be tested in the volume and following the procedures prescribed in § 630.35(a)(5), and the virus pool is satisfactory only if there is no evidence of adventitious agents.

(6) *Bacteriological tests.* In addition to the tests for sterility required pursuant to § 610.12 of this chapter, bacteriological tests shall be performed on each mumps virus pool for the presence of M. tuberculosis, both avian and human, by appropriate culture methods. The virus pool is satisfactory only if found negative for M. tuberculosis, both avian and human.

(7) *Test for avian leucosis.* If the cultures were not derived from a certified source and control fluids were not tested for avian leucosis, the vaccine shall be tested in the volume and following the procedures prescribed in § 630.35(a)(8). The cultures are satisfactory for vaccine manufacture if found negative for avian leucosis.

(b) *Clarification.* The mumps virus fluids shall be clarified by following the procedures prescribed in § 630.35(c).

[38 FR 32068, Nov. 20, 1973, as amended at 55 FR 47876, Nov. 16, 1990]

§ 630.56 General requirements.

(a) *Final container tests.* In addition to the tests required pursuant to § 610.14 of this chapter, an immunological and virological identity test shall be performed on the final container if it was not performed on each pool or the bulk vaccine prior to filling.

(b) *Dose.* These standards are based on an individual human immunizing dose of no less than 5,000 $TCID_{50}$ of Mumps Virus Vaccine Live, expressed in terms of the assigned titer of the Reference Mumps Virus, Live.

(c) *Labeling.* In addition to the items required by other applicable labeling provisions of this part, single dose container labeling for vaccine which is not protected against photochemical deterioration shall include a statement cautioning against exposure to sunlight.

(d) [Reserved]

(e) *Photochemical deterioration; protection.* Mumps Virus Vaccine Live, in multiple dose containers, shall be protected against photochemical deterioration in accordance with the procedures prescribed in § 630.36(g).

(f) *Samples and protocols.* For each lot of vaccine, the following materials shall be submitted to the Director, Center for Biologics Evaluation and Research, Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892:

(1) A protocol which consists of a summary of the history of manufacture of each lot including all results of each test for which test results are requested by the Director, Center for Biologics Evaluation and Research.

(2) A total of no less than two 25-milliliter volumes, in a frozen state (−60° C), of preclarification bulk vaccine containing no preservative, stabilizer, or adjuvant.

(3) A total of no less than 30 containers of the vaccine from each filling of each bulk lot of single-dose containers. A total of no less than six 50-dose containers or ten 10-dose containers of the vaccine from each filling of each bulk lot of multiple-dose containers.

[38 FR 32068, Nov. 20, 1973, as amended at 39 FR 9661, Mar. 13, 1974; 41 FR 10429, Mar. 11, 1976; 49 FR 23834, June 8, 1984; 50 FR 4138, Jan. 29, 1985; 51 FR 15610, Apr. 25, 1986; 55 FR 11013, Mar. 26, 1990]

Subpart G—Rubella Virus Vaccine Live

§ 630.60 Rubella Virus Vaccine Live.

(a) *Proper name and definition.* The proper name of this product shall be Rubella Virus Vaccine Live, which shall consist of a preparation of live, attenuated rubella virus.

(b) *Criteria for acceptable strains of attenuated rubella virus.* Strains of attenuated rubella virus used in the manufacture of vaccine shall be identified by (1) historical records including origin and manipulation during attenuation and (2) antigenic specificity as rubella virus as demonstrated by tissue culture neutralization tests.

(c) *Extraneous agents.* Seed virus used for vaccine manufacture shall be free of all demonstrable extraneous viable microbial agents except for unavoidable bacteriophage.

(d) *Field studies with experimental vaccines.* (1) Strains used for the manufacture of Rubella Virus Vaccine Live, shall have been shown in field studies with experimental vaccines to be safe and potent in the group of individuals inoculated, which must include at least 10,000 susceptible individuals. Susceptibility shall be shown by the absence of neutralizing or hemagglutination-inhibiting antibodies against rubella virus or by other appropriate methods.

(2) The virus strain used in the field studies shall be propagated in the same cell culture system that will be used in the manufacture of the product.

(3) The field studies shall be so conducted that at least 5,000 of the susceptible individuals must reside when inoculated in areas where health related statistics are regularly compiled in accordance with procedures such as those used by the National Center for Health Statistics. Data in such form as will identify each inoculated person shall be furnished to the Director, Center for Biologics Evaluation and Research.

(4) Inoculated persons shall be shown not to be contagious for contacts through surveillance of rubella susceptible contacts of the inoculated persons.

(e) *Neurovirulence safety test of the virus seed strain in monkeys*—(1) *The test.* A demonstration shall be made in monkeys of the lack of neurotropic properties of the seed strain of attenuated rubella virus used in the manufacture of rubella vaccine. For this purpose and to establish consistency of manufacture of the vaccine, vaccine from each of five consecutive lots shall be tested separately in monkeys shown to be serologically negative for rubella virus antibodies in the following manner:

(i) A test sample of vaccine removed after clarification but before final dilution for standardization of virus content shall be used for the test.

(ii) Vaccine shall be injected by combined intracerebral, intraspinal, and intramuscular routes into not less than 20 Macaca or Cercopithecus monkeys or a species found by the Director, Center for Biologics Evaluation and Research, to be equally suitable for the purpose. The animals shall be in overt